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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/594,978	06/15/2000	Varghese John	00270-US-NEW	8679

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EXAMINER
LUKTON, DAVID

ART UNIT	PAPER NUMBER
1653	18

DATE MAILED: 05/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/594,978	JOHN ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6,8-16,19,20,23,47,50-52,54-62,65,66 and 69-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,4-6,8-16,19,20,23 and 70-72* is/are allowed.

6)☒ Claim(s) *47,50-52,54-62,65,66,69 and 73-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

The claims were last amended pursuant to the directives of paper No. 13 (filed 10/31/02), Claims 1, 4-6, 8-16, 19, 20, 23, 47, 50-52, 54-62, 65, 66, 69-75 remain pending. Applicants' arguments filed 10/31/02 have been considered and found persuasive in part. With the exception of the §112, first paragraph rejection, the previously imposed rejections are withdrawn. Claims 1, 4-6, 8-16, 19, 20, 23, 70-72 are now characterized as allowable.

*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47, 50-52, 54-62, 65, 66, 69, 73-75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 47 is drawn to a "pharmaceutical" composition. This term implies an assertion of therapeutic efficacy, which is not in evidence. In response, applicants have argued that the term "pharmaceutical" has long been accepted in patent claims, and that more than 13,000 patents recite the phrase "pharmaceutical composition" in the claims. Applicants have

further argued that the term "pharmaceutical" does not imply an assertion of therapeutic efficacy. With respect to this latter point (that of an implied assertion), there are two possibilities: (a) applicants really do not intend to imply that the compositions are effective to treat Alzheimer's Disease, or any other disease, or (b) applicants do want to imply that the compositions are effective to treat one or more human diseases. Those are really the only two possibilities. If it is really true that applicants have no interest in asserting (in the claims) that the compounds are effective to treat a human disease, then applicants should feel no reluctance in deleting the term at issue (i.e., the term "pharmaceutical"). If, on the other hand, applicants really do want to make such an assertion (in the claims) then applicants can at least understand the basis of the rejection (though it may be traversed). Whether the term "pharmaceutical" is "accepted" or "not accepted" does not change the foregoing analysis.

As indicated above, applicants have argued that the term "pharmaceutical" is "accepted" by patent examiners. Where matters of law are concerned, however, the issue is usually not simply that of acceptability versus unacceptability. The issue, instead, is compliance with the law. For almost any violation of the civil code (for example), there exist some people who believe that the law in question should not be enforced. If a person is driving a car at a speed of 70 mph in a 55 mph zone, this constitutes a violation of the law. Some might find this course of action to be acceptable; others will find it unacceptable. But the

fact remains that driving (a car) over the speed limit is a violation of the law. Turning back to the specific issue at hand, it is true that many examiners have abstained from imposing an enablement rejection against claims drawn to pharmaceutical compositions. Among the 13,000 patents referred to by applicants, there are no doubt many applicants among them who never provided evidence of therapeutic efficacy, and the examiner merely abstained from imposing an enablement rejection. In other cases (of the 13,000), the applicants did provide evidence of therapeutic efficacy. However, the fact that some examiners have abstained from imposing an enablement rejection in other applications does not mean that such a rejection is improper in the instant case. As indicated above, the term "pharmaceutical" implies an assertion of therapeutic efficacy. This is not to say that "pharmaceutical composition" claims are identical in all respects with therapeutic method claims. However, from the perspective of enablement, there is considerable overlap of the issues. As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims.

What applicants have shown is that if one of the claimed compounds is added to a complex

mixture which applicants believe contains *beta*-secretase, some inhibition of hydrolysis of a derivative of the peptide Sta-Val-Ala-Glu-Phe can be achieved. Perhaps inhibition of amyloid formation would occur *in vivo* (following administration), and perhaps not. But even if some inhibition of amyloid formation could be achieved, this would not necessarily translate into a treatment for Alzheimers Disease (or Down's Syndrome, hereditary cerebral hemorrhage with amuyloidosis of the Dutch type). One of the issues is the criticality of the amyloid protein. Does the occurrence of Alzheimers Disease depend solely and exclusively on the presence of amyloid protein? While amyloid protein no doubt plays a role, the degree of criticality of this protein has not been established. Then there is the question of administering the compounds to a patient with established Alzheimer's Disease, in whose brain significant amyloid protein has already been deposited. Can a reversal of the adverse effects of this protein be achieved merely be inhibiting further formation? In addition, there is the question of the degree of inhibition. If the amyloid protein is being deposited at the rate of 100 "units" per month in the absence of the claimed compound, and 90 "units" per month in the presence of the claimed compound, one can say that inhibition has occurred. But in such a situation, the patients' condition will only worsen, and therapeutic efficacy will not have been achieved. If therapeutic efficacy cannot be achieved by a given composition, one cannot justify the characterization of that composition as a "pharmaceutical" composition.

As for the matter of "unpredictability", Steinberg (*The Scientist* **16**, 22, 2002) has disclosed that when researchers vaccinated transgenic mice that had developed AD-like pathology, placques "melted away". In addition, favorable results were obtained in cognitive experiments with the mice. However, when attempted in humans, the Alzheimer's symptoms worsened. This reference supports the proposition that even if one can obtain apparently favorable results in rats, one cannot "predict" therapeutic efficacy in humans. Applicants, for their part, have not even taken the step of showing any *in vivo* effect in a test animal, to say nothing of a potential therapeutic effect.

In accordance with the foregoing, "undue experimentation" would be required to determine whether, and under what conditions, the claimed compositions can be used to treat human diseases. It is suggested that the term "pharmaceutical" be deleted from the claims which recite it.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

DAVID LUKTON
PATENT EXAMINER
GROUP 1600